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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: De Corte, et al. **Filed: November 1, 1999**

Patent No.: 6,878,717 **Application No.: 09/430,966**

Issued: April 12, 2005 **Patentee: Janssen Pharmaceutica, N.V.**

For: HIV REPLICATION INHIBITING PYRIMIDINES

MAIL STOP EX PARTE REEXAM
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REQUEST FOR *EX PARTE* REEXAMINATION PURSUANT TO 37 CFR § 1.510

☒ This is a Request for Reexamination of patent number **6,878,717** issued **April 12, 2005**.

☒ The name and address of the person requesting reexamination is **JANSSEN PHARMACEUTICA, N.V., TURNHOUTSEWEG 30, B2340 BEERSE, BELGIUM**.

☒ Reexamination of claim(s) **1-5** is requested.

☐ An English language translation of all necessary and pertinent non-English language patents or printed publications is included.

☒ The attached detailed request includes at least the following items:

- ☒ A statement identifying each substantial new question of patentability based on prior patents and printed publications. 37 CFR § 1.510(b)(1).
- ☒ An identification of every claim for which reexamination is requested, and a detailed explanation of the pertinency and manner of applying the cited prior art to every claim for which reexamination is requested. 37 CFR § 1.510(b)(2).
- ☒ A copy of every patent or printed publication relied upon is submitted herewith including a listing thereof on form PTO-1449. 37 CFR § 1.510(b)(3).

☒ A copy of the patent to be reexamined or a permanent reproduction thereof in double column format of the printed patent securely mounted on one side of a separate paper is enclosed. 37 CFR § 1.510(b)(4).

☐ A copy of any disclaimer, certificate of correction or reexamination certificate issued in the patent is included. 37 CFR § 1.510(b)(4).

☐ It is certified that a copy of this request (if filed by other than the patent owner) has been served in its entirety on the patent owner as provided in 37 CFR § 1.33(c). The name and address of the party served and the date of service are:

☐ A proposed amendment is included (only where the patent owner is the requester). 37 CFR § 1.510(e).

☐ A check in the amount of **$ .00** is attached. Please charge any deficiency or credit any overpayment to Deposit Account 23-3050.

☒ Please charge Deposit Account No. 23-3050 in the amount of **$2,520.00**.

☒ The Commissioner is hereby requested to grant an extension of time for the appropriate length of time, should one be necessary, in connection with this filing or any future filing submitted to the U.S. Patent and Trademark Office in the above-identified application during the pendency of this application. The Commissioner is further authorized to charge any fees related to any such extension of time to Deposit Account 23-3050.

Name and address of party served:

Date of Service ; or

☐ A duplicate copy is enclosed because service was not possible.

☒ The requester's correspondence address (if different than above) is **Customer Number 45511** which is **Woodcock Washburn LLP, Cira Centre, 12th Floor, 2929 Arch Street, Philadelphia, PA 19104-2891**

DETAILED REQUEST FOR REEXAMINATION

Janssen Pharmaceutica N.V. ("the Patent Owner") respectfully requests reexamination of claim 1 of U.S. Patent No. 6,878,717 ("the 717 Patent"; attached hereto as Appendix A) which issued on April 12, 2005, in the names of Bart De Corte, Marc Rene De Jonge, Jan Heeres, Chih Yung Ho, Paul Adriaan Jan Janssen, Robert W. Kavash, Lucien Maria Henricus Koymans, Michael Joseph Kukla, Donald William Ludovici, and Koen Jeanne Alfons Van Aken.

I. Statement Identifying Each Potential Substantial New Question of Patentability Based on Prior Patent And Printed Publications

This Request for Reexamination is filed in view of three issued patents, U.S. Pat. Nos. 6,200,977 (attached hereto as Appendix B), 6,528,513 (attached hereto as Appendix C), and 6,835,726 (attached hereto as Appendix D), each said to be directed to pyrimidine derivatives that can be used for the treatment of viral infections, and each claiming priority to a provisional application filed in the United States prior to the earliest filing date currently claimed by the 717 Patent.

These documents arguably raise a question as to the validity of claims 1-5 of the 717 Patent.

II. Identification of Claims For Which Reexamination Is Requested

Reexamination is requested with respect to claims 1-5 of the 717 Patent.

III. Detailed Explanation Of The Pertinency Of The Documents To The Claims

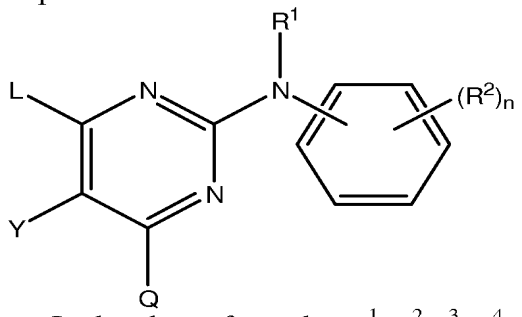
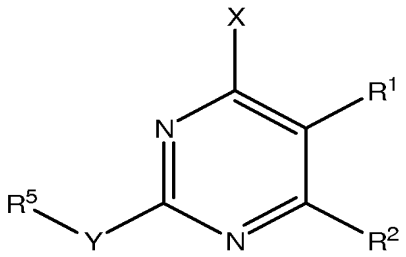
The claimed inventions are based, in part, on the novelty of the disclosed pyrimidine derivatives and the discovery that these compounds can be used for the treatment of viral infections, including infections by Human Immunodeficiency Virus (HIV) in human subjects.

U.S. Pat. Nos. 6,200,977 ("the 977 Patent"), 6,528,513 ("the 513 Patent"), and 6,835,726 ("the 726 Patent") each claim priority to a provisional application (U.S. Prov. App. No. 60/075,005) that was filed in the United States prior to the earliest filing date currently claimed by the 717 Patent. These patents disclose pyrimidine derivatives that can be used for the treatment of viral infections. Due to arguable similarity between the disclosed compounds and those recited in the 717 Patent claims, a question is raised as to whether the subject matter of claims 1-5 would have been obvious under 35 U.S.C. § 103(a).

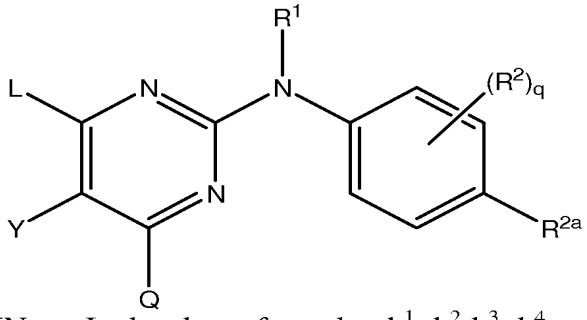
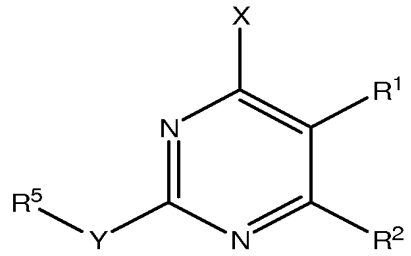
Table 1, below, provides a comparison of the potentially relevant portions of the disclosures of the 977 Patent, the 513 Patent, and the 726 Patent[1] with the relevant portions of claims 1-5 of the 717 Patent.

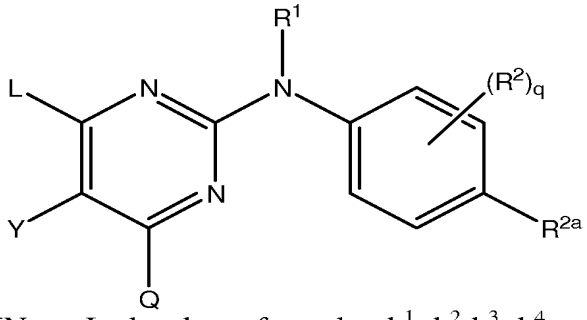
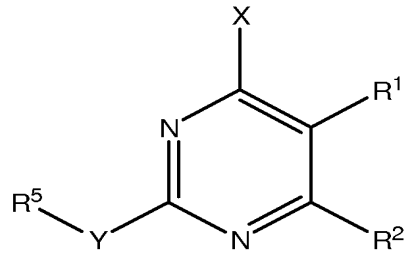
[1] Although the respective disclosures of the 977 Patent, the 513 Patent, and the 726 Patent appear to be substantively alike, all column and line references correspond to the 977 Patent.

TABLE 1

717 Patent Claim	977 Patent / 513 Patent / 726 Patent Disclosure
1. A method of treating subjects suffering from HIV (Human Immunodeficiency Virus) infection comprising administering to the subject a therapeutically effective amount of a compound of formula:  [Note: In the above formula, -a^1=a^2-a^3=a^4- appears as (a-1) for ease of reference] wherein n is 0, 1, 2, 3, or 4; R^1 is hydrogen, aryl, or C_{1-6} alkyl; Each R^2 is independently hydroxy, halo, C_{1-6} alkyl optionally substituted with cyano or –C(=O)R^6, C_{1-6} alkloxy, cyano, nitro, amino, or mono- or di(C_{1-6} alkyl)amino; L is C_{1-10}alkyl, phenyl, pyridinyl, or –X–R^3; wherein R^3 is phenyl; X is –NR^1– , –NH–NH–, –S–, or –O–; Q represents hydrogen, C_{1-6} alkyl, halo, or –NR^4R^5; R^4 and R^5 are each independently selected from hydrogen, C_{1-12} alkyl, or aryl; Y represents halo, C_{1-6} alkyl substituted with cyano, C_{1-6} alkyloxy, cyano, nitro, amino, mono- or di(C_{1-6} alkyl)amino, or aryl	"The compounds have the general formula I":  (I) (col. 1, line 67 through col. 2, line 10) in which X represents –SR^3 or alkyl (col. 2, line 11) Y represents –N(R^6)– (col. 2, lines 12-13) R^1 and R^2 are independently selected from alkyl, -O-alkyl, aryl, -NO_2, -NR^7R^8, -CN, halogen (col. 2, lines 14-18) R^3 is aryl (col. 2, lines 19-20); R^5 and R^6 are independently hydrogen, alkyl, or aryl (col. 2, lines 24-25) R^7 and R^8 are each independently hydrogen or alkyl (col. 2, lines 25-26) Substituents for the alkyl groups can be –CN (col. 4, line 61 & col. 5, line 3) Substituents for the aryl groups can be halo, –OR′, or –CN (col. 5, lines 16-18) R′ can be hydrogen or (C1-C8)alkyl (col. 5, lines 24-25)

717 Patent Claim	977 Patent / 513 Patent / 726 Patent Disclosure
2. The method of claim 1, wherein R^1 is hydrogen, aryl, or C_{1-6} alkyl	Y represents $-N(R^6)-$ (col. 2, lines 12-13) R^6 can be hydrogen, alkyl, or aryl (col. 2, lines 24-25) R^5 can be hydrogen, alkyl, or aryl (col. 2, lines 24-25)

717 Patent Claim	977 Patent / 513 Patent / 726 Patent Disclosure
3. A method of treating non-nucleoside reverse transcriptase inhibitor resistant HIV infection in a subject in need thereof comprising administering to the subject an effective amount of a compound having the formula:  [Note: In the above formula, -b^1=b^2-b^3=b^4- appears as (b-1) for ease of reference] wherein q is 0, 1, 2, 3, or 4; R^1 is hydrogen, aryl, or C_{1-6} alkyl; Each R^2 is independently hydroxy, halo, C_{1-6} alkyl optionally substituted with cyano or –C(=O)R^6, C_{1-6} alkloxy, cyano, nitro, amino, or mono- or di(C_{1-6} alkyl)amino; L is C_{1-10}alkyl, phenyl, pyridinyl, or –X–R^3; wherein R^3 is phenyl; X is –NR^1– , –NH–NH–, –S–, or –O–; Q represents hydrogen, C_{1-6} alkyl, halo, or –NR^4R^5; R^4 and R^5 are each independently selected from hydrogen, C_{1-12} alkyl, or aryl; Y represents halo, C_{1-6} alkyl substituted with cyano, C_{1-6} alkyloxy, cyano, nitro, amino, mono- or di(C_{1-6} alkyl)amino, or aryl, and R^{2a} is cyano.	"The compounds have the general formula I":  (I) (col. 1, line 67 through col. 2, line 10) in which X represents –SR^3 or alkyl (col. 2, line 11) Y represents –N(R^6)– (col. 2, lines 12-13) R^1 and R^2 are independently selected from alkyl, -O-alkyl, aryl, -NO_2, -NR^7R^8, -CN, halogen (col. 2, lines 14-18) R^3 is aryl (col. 2, lines 19-20); R^5 and R^6 are independently hydrogen, alkyl, or aryl (col. 2, lines 24-25) R^7 and R^8 are each independently hydrogen or alkyl (col. 2, lines 25-26) Substituents for the alkyl groups can be –CN (col. 4, line 61 & col. 5, line 3) Substituents for the aryl groups can be halo, –OR′, or –CN (col. 5, lines 16-18) R′ can be hydrogen or (C1-C8)alkyl (col. 5, lines 24-25)

717 Patent Claim	977 Patent / 513 Patent / 726 Patent Disclosure
4. A method of treating non-nucleoside reverse transcriptase inhibitor resistant HIV-1 infection in a subject in need thereof comprising administering to the subject an effective amount of a compound having the formula:  [Note: In the above formula, -b^1=b^2-b^3=b^4- appears as (b-1) for ease of reference] wherein q is 0, 1, 2, 3, or 4; R^1 is hydrogen, aryl, or C_{1-6} alkyl; Each R^2 is independently hydroxy, halo, C_{1-6} alkyl optionally substituted with cyano or –C(=O)R^6, C_{1-6} alkloxy, cyano, nitro, amino, or mono- or di(C_{1-6} alkyl)amino; L is C_{1-10}alkyl, phenyl, pyridinyl, or –X–R^3; wherein R^3 is phenyl; X is –NR^1– , –NH–NH–, –S–, or –O–; Q represents hydrogen, C_{1-6} alkyl, halo, or –NR^4R^5; R^4 and R^5 are each independently selected from hydrogen, C_{1-12} alkyl, or aryl; Y represents halo, C_{1-6} alkyl substituted with cyano, C_{1-6} alkyloxy, cyano, nitro, amino, mono- or di(C_{1-6} alkyl)amino, or aryl, and R^{2a} is cyano.	"The compounds have the general formula I":  (I) (col. 1, line 67 through col. 2, line 10) in which X represents –SR^3 or alkyl (col. 2, line 11) Y represents –N(R^6)– (col. 2, lines 12-13) R^1 and R^2 are independently selected from alkyl, -O-alkyl, aryl, -NO_2, -NR^7R^8, -CN, halogen (col. 2, lines 14-18) R^3 is aryl (col. 2, lines 19-20); R^5 and R^6 are independently hydrogen, alkyl, or aryl (col. 2, lines 24-25) R^7 and R^8 are each independently hydrogen or alkyl (col. 2, lines 25-26) Substituents for the alkyl groups can be –CN (col. 4, line 61 & col. 5, line 3) Substituents for the aryl groups can be halo, –OR′, or –CN (col. 5, lines 16-18) R′ can be hydrogen or (C1-C8)alkyl (col. 5, lines 24-25)

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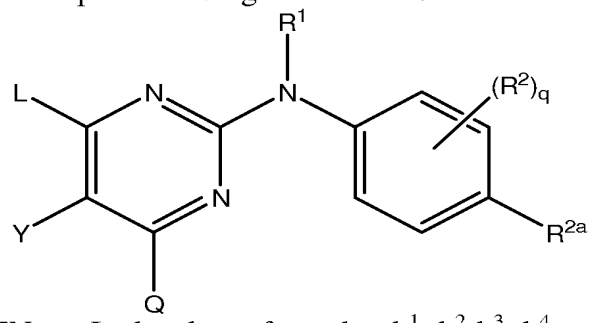
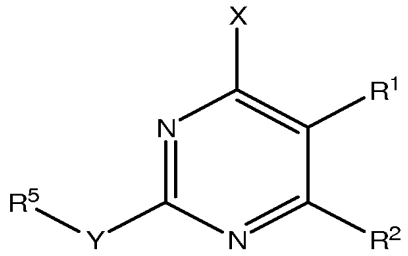
5. A method of treating subjects suffering from HIV (Human Immunodeficiency Virus) infection comprising administering to the subject a therapeutically effective amount of a compound having the formula:  [Note: In the above formula, -b^1=b^2-b^3=b^4- appears as (b-1) for ease of reference] wherein q is 0, 1, 2, 3, or 4; R^1 is hydrogen, aryl, or C_{1-6} alkyl; Each R^2 is independently hydroxy, halo, C_{1-6} alkyl optionally substituted with cyano or –C(=O)R^6, C_{1-6} alkloxy, cyano, nitro, amino, or mono- or di(C_{1-6} alkyl)amino; L is C_{1-10}alkyl, phenyl, pyridinyl, or –X–R^3; wherein R^3 is phenyl; X is –NR^1– , –NH–NH–, –S–, or –O–; Q represents hydrogen, C_{1-6} alkyl, halo, or –NR^4R^5; R^4 and R^5 are each independently selected from hydrogen, C_{1-12} alkyl, or aryl; Y represents halo, C_{1-6} alkyl substituted with cyano, C_{1-6} alkyloxy, cyano, nitro, amino, mono- or di(C_{1-6} alkyl)amino, or aryl, and R^{2a} is cyano.	"The compounds have the general formula I":  (I) (col. 1, line 67 through col. 2, line 10) in which X represents –SR^3 or alkyl (col. 2, line 11) Y represents –N(R^6)– (col. 2, lines 12-13) R^1 and R^2 are independently selected from alkyl, -O-alkyl, aryl, -NO_2, -NR^7R^8, -CN, halogen (col. 2, lines 14-18) R^3 is aryl (col. 2, lines 19-20); R^5 and R^6 are independently hydrogen, alkyl, or aryl (col. 2, lines 24-25) R^7 and R^8 are each independently hydrogen or alkyl (col. 2, lines 25-26) Substituents for the alkyl groups can be –CN (col. 4, line 61 & col. 5, line 3) Substituents for the aryl groups can be halo, –OR′, or –CN (col. 5, lines 16-18) R′ can be hydrogen or (C1-C8)alkyl (col. 5, lines 24-25)

IV. Conclusion

The Patent Owner respectfully requests that the PTO confirm whether it is of the view that the documents cited on form PTO-1449, filed herewith, raise any substantial new issue of patentability with respect to claims 1-5 of the 717 Patent.

Date: December 12, 2007

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